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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/935,290	08/21/2001	Rosana Kapeller-Libermann	MNI-186	8801

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Intellectual Property Group
MILLENNIUM PHARMACEUTICALS INC.
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EXAMINER	
NASHED, NASHAAT T	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 01/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/935,290	KAPELLER-LIBERMANN ET AL.	
	Examiner	Art Unit	
	Nashaat T. Nashed	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *29 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The application has been amended as requested in the communication filed December 29, 2003. Accordingly, claims 12-43 have been canceled, and claim 4 has been amended.

Applicant's election without traverse of Group I, claims 1-7 and 12 in Paper No. 12 is acknowledged.

Claims 1-11 are under consideration in this Office

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see for example page 81, line 35. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

Applicants disclose a nucleic acid sequence of SEQ ID NO: 1 (SEQ ID NO: 3 is the coding region of SEQ ID NO: 1) comprising an open reading frame encoding the amino acid sequence of SEQ ID NO: 2. The application indicates that the polypeptide of SEQ ID NO: 2 is sought to be an acyltransferase based on the observation of reasonable sequence homology between the amino acid sequence of SEQ ID NO: 2 and a known acyltransferase in the prior art. While the acyltransferase is accepted as a plausible and credible asserted utility, it is not a specific or substantial utility. One of ordinary skill in the art would not know which acyl group is being transferred and to what acceptor. Since human produces many acyltransferases for many purposes included those referred to in the Background section of the specification, each acyltransferase is expected to have a specific substrates and function. The specification describes non-specific utilities for the protein, nucleic acid, and antibodies. The nucleic acid is said to be used in a method to detect a human gene and to recombinantlly make the polypeptide of SEQ ID NO: 2 which neither the gene nor the polypeptide are associated with a specific use or a disease. The mere fact that the polypeptides disclosed in the specification is called 56919, a novel human acyltransferase is indicative that the applicants have no idea about the specific

utility of the protein of SEQ ID NO: 2 or the nucleic acid sequences of SEQ ID NO's: 1 and 3 at the time they filed their application. It appears that the main utility of the polypeptide and nucleic acid is to carry out further research to identify the biological function and possible diseases associated with said function. Substantial utility defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utility. Thus, the claimed invention has no specific or substantial asserted utility.

Applicant is referred to the revised interim guidelines concerning compliance with utility requirement of 35 U.S.C. 101, published in the Official Gazette and also available at www.uspto.gov.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 3, and 4-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 3 is directed to all possible DNAs encoding any naturally occurring allelic variants to SEQ ID NO: 2. Claim 4 directed to (a) a nucleic acid which is 90% identical to SEQ ID NO's: 1 and 3; (b) a nucleic acid comprising 150 nucleotide of SEQ ID NO: 1 or 3; (c) a nucleic acid encoding a polypeptide having 90% identical to the polypeptide of SEQ ID NO: 2; and (d) a nucleic acid encoding a polypeptide comprising 50 contagious amino acid residues of SEQ ID NO: 2. Claim 5 is drawn to any nucleic acid sequence that hybridizes to the nucleic acid sequence of any of claims 3 and 4 under any stringent conditions. The specification, however, only provides a single representative species from human encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these DNAs by any identifying structural

characteristics or properties other than the sequence identification numbers recited in the claims, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 3-11 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling for the claims limited. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to all possible nucleic acid sequences encoding variants of SEQ ID NO: 2, those having 90% sequence identity with SEQ ID NO's: 1 or 3, those encoding an amino acid sequence that is 90% identical to SEQ ID NO: 2, those comprising a 150 nucleotide, presumably, contagious of SEQ ID NO: 1 or 3, and those encoding a polypeptide comprising 50 contagious amino acid residue of SEQ ID NO: 2. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses all possible nucleic acid sequences encoding variants of SEQ ID NO: 2, those having 90% sequence identity with SEQ ID NO's: 1 or 3, those encoding an amino acid sequence that is 90% identical to SEQ ID NO: 2, those comprising a 150 nucleotide, presumably, contagious of SEQ ID NO: 1 or 3, and those encoding a polypeptide comprising 50 contagious amino acid residue of SEQ ID NO: 2. The specification provides guidance and examples in the form of an assay to identify the nucleic acid of SEQ ID NO: 1 and 3 as well as the amino acid sequence of SEQ ID NO: 2. While molecular biological techniques and genetic manipulation to make any nucleic acid sequence are known in the prior art and the skill of the artisan are well developed, knowledge regarding a specific substrates for the presumed acyltransferase of SEQ ID NO: 2, biological function(s), methods of redesigning 10% of the amino acid residue to a functional structure or *de novo* design a polypeptide having any specific function around 50 contagious amino acid residue of SEQ ID NO: 2, and the biological source of those nucleic acid sequence claimed in claims 3-5 is lacking. Thus, searching for a nucleic acid sequence having any specific utility is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation to identify said nucleic acid is enormous. Since routine experimentation in the art does not include screening large number of genomic and cDNA libraries prepared from large number of organism or man-made mutant libraries made from

the nucleic acid sequences of SEQ ID NO's: 1 or 3 where the expectation of obtaining the desired nucleic acid with the intended specific utility is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the biological source of the nucleic acid, the chemical of biological function of the polypeptide of SEQ ID NO: 2, the three dimensional structure of the polypeptide of SEQ ID NO: 2, and the amino acid residues which can be substituted, deleted, and/or inserted without loss of the desired activity. Without such a guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 5 and 6-11 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) The phrase "a naturally-occurring allelic variant" in claim 3 render the claims indefinite because the resulting claim does not set fourth the metes and bounds of the desired patent protection. The phrase is found indefinite and confusing because the specification does not define the phrase and one of ordinary skill in the art could not distinguish the difference between a naturally occurring nucleic acid and a man-made one. For examination purposes only, the phrase is taken to mean a homolog of SEQ ID NO: 2.

(b) The phrase "stringent conditions" in claim 5 renders the claim indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Since there are several hybridization conditions known in the art as "stringent conditions" and the result of a hybridization experiment will vary with each set of "stringent conditions", the claim is found indefinite. Identifying a specific hybridization and wash conditions in the claim would obviate this rejection.

(c) Claims 6-11 are included in this rejection because they are dependent on a rejected claims and do not cure their deficiencies.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-6, 8 and 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Shin *et al.* (J. Biol. Chem. 1991, 266 (35), 23834-23839).

Shin *et al.* teach the murine nucleic acid sequence encoding an acyltransferase, see the abstract and Figure 3. The nucleic acid sequence taught by Shin *et al.* is 63% and 74.8% identical to SEQ ID NO: 1 and 3, respectively, of the instant application, and would be expected to hybridize under some stringent condition to both SEQ ID NO's: 1 and 3 (claim 5). The amino acid sequence taught by Shin *et al.* has 93% sequence identity to SEQ ID NO: 2 and could be considered a naturally-occurring allelic variant of SEQ ID NO: 2 (claim 3). It comprises several stretches of contagious amino acid residues of 50 or more residues. For example, residues 185-262 (78 residues), 502-551 (50 residues), and the last 71 residues of SEQ ID NO: 2 are found in the sequence taught by Shin *et al.* (claims 4 and 6). Also, Shin *et al.* teach the construction of vector and host cell comprising the nucleic acid sequence (claims 8 and 10), see the experimental section, the paragraph bridging pages 23834 and 23835.

Claims 3-6 and 8-11 is rejected under 35 U.S.C. 102(b) as being anticipated by Bhat *et al.* (Biochim. Bioph. Acta **(August 8, 1999)** 1439, 415-423. The reference has been available on line since August 13, 1999.

Bhat *et al.* teach a nucleic acid sequence encoding a rat *sy*-glycerol-3-phosphate acytransferase, see the abstract and Figure 1. The amino acid and nucleic sequences taught by the reference are 92.4% and 75% homologous to SEQ ID NO's: 2 and 3, respectively, of the instant application. The nucleic acid sequence taught by Bhat *et al.* would be expected to hybridize under some stringent condition to both SEQ ID NO's: 1 and 3 (claim 5). The amino acid sequence taught by Bhat *et al.* is considered a naturally - occurring allelic variant of SEQ ID NO: 2 (claim 3). It comprises several stretches of contagious amino acid residues of 50 or more residues (claims 4 and 6). Also, Bhat *et al.* teach the construction of an expression vector and transforming insect host cell comprising the nucleic acid sequence (claims 8-10) as well as the use of a host cell to produce the enzyme in large quantity (claim 11), see page 421, left column, paragraph 2.

Claims 4, 5, 6, 8, and 10 is rejected under 35 U.S.C. 102(a) as being anticipated by Hegde *et al.* (Database: EST, Accession number: AW976326).

Hegde *et al.* teach a nucleic acid sequence of 568 base which is 97% homologous to residues 2229-2796 of SEQ ID NO: 1, and contains over 450 contagious nucleotide of SEQ ID NO: 1 (claim 4). It is available in a vector comprised in host cell (claim 8 and 10).

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 7 and 11 are rejected under 35 U.S.C. § 103 as being unpatentable over Bhat *et al.* in view of the state of the prior art with regard to preparing protein as fusion protein for easy purification.

The teaching of Bhat *et al.* is summarized above.

Bhat *et al.* provide one of ordinary skill in the art at the time of invention with motivation to develop a recombinant method to produce the glycerol-3-phosphate acyltransferase in large quantity with high purity. They teach the regulation of said enzyme may be critical during metabolic transition between fasting and refeeding and in the development of complex metabolic disorders such as obesity, diabetes mellitus, and atherosclerosis, see the paragraph bridging the right and left columns on page 415. Thus,

it would have been obvious to one of ordinary skill in the art at the time of invention to fuse the coding region of the enzyme taught by Bhat *et al.* to the coding region of an affinity binding domain such as the maltose binding protein of *E. coli*, glutathione S-transferase, or the 6-His Tag by well known methods in the art (claim 7), insert the resulting nucleic acid in a vector, transform a host cell and express the fusion protein, purify the recombinantly produced protein by affinity chromatography, and remove the affinity tag by chemical or enzymatic methods by well known methods in the art to produce the purified protein (claim 11). Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, clearly *prima facie* obvious.

The art made of record and not relied upon is considered pertinent to the applicant disclosure.

(1) US 2003/0165831 (published 9/4/03) contain the nucleic acid sequence of SEQ ID NO: 20793 which comprised the entire nucleic acid sequence of SEQ ID NO: 3 of the instant application. The published U. S. application 09/814,353, filed 3/21/01 claims priority to provisional application 60/191,031, filed 3/21/00; 60/207,124, filed 5/25/00; and 60/211,940, filed 6/15/00. The examiner was unable to identify or link SEQ ID NO: 20793 to any of the priority documents.

(2) WO 01/60860 (published 8/23/01) based on PCT/US01/05171 application, filed 2/2/01 which claim priority to 60/183,319, filed 2/17/00; 60/189,862, filed 3/16/00; 60/207,454, filed 5/25/00; 60/211,314 filed 6/9/00;60/219,007, filed 7/18/00; and 60/255,281 filed 12/13/00. The WO document contain a nucleic acid sequence, identified as human prostate expression marker cDNA 25304 that is identical to SEQ ID NO: 3 of the instant application. The examiner could not identify the said sequence with a sequence identification number and thus, was unable to identify the sequence in any of the provisional applications cited above.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday and Friday from 9:00 a.m. to 5:30 p.m. The examiner is expected to move to the new Patent and Trademark Office facility in Alexandria, VA on January 22, 2004. The new telephone number for the examiner will be 571-272-0934.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph. D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-7401. Effective January 22, 2004 Dr. Achutamurthy telephone number will be 571-272-0928.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nashaat T. Nashed, Ph. D.
Primary Examiner